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Pars Plana Vitrectomy for the treatment of tractional and degenerative lamellar macular holes: functional and anatomical results.

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Abstract:	Purpose: Functional and anatomic outcomes of vitrectomy with membrane peeling were compared in tractional lamellar macular holes (LMH)/Macular pseudoholes (MPH) versus degenerative LMH. Methods: This multicenter retrospective study enrolled patients with a minimum follow-up of 6 months. The association of spectral-domain optical coherence tomography (SD-OCT) parameters with pre- and postoperative best-corrected visual acuity (BCVA) was analyzed. Results: Seventy-seven (74.8%) tractional LMH/MPH, and 26 (25.2%) degenerative LMH were included. Preoperative BCVA was better in tractional LMH/MPH (0.39±0.2 logMAR, 20/50 Snellen Equivalent) than degenerative LMH (0.56±0.2 logMAR, 20/66 Snellen Equivalent; p<0.001). Premacular membranes (PMM) were found in all tractional LMH/MPH, while LMH associated epiretinal proliferation (LHEP) was present in all degenerative LMH. Primary anatomic success was achieved in 97/103 eyes (94.2%), with foveal restoration occurring earlier in degenerative LMH (1.6±2.3 VS 3.3±3.6 months; p=0.025). BCVA improved in both tractional LMH/MPH and degenerative LMH (p<0.001 and p=0.012, respectively), but was better in tractional LMH/MPH (p=0.001). Conclusions: The presence of PMM and absence of LHEP in all tractional LMH/MPH further distinguishes this from degenerative LMH. BCVA improved in both subgroups, but more so in tractional LMH/MPH. Complete anatomic restoration of foveal

Pars Plana Vitrectomy for the treatment of tractional and degenerative lamellar macular holes: functional and anatomical results.

Short title: Surgery for lamellar macular holes.

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Tractional Lamellar Macular Hole; Macular Pseudohole; Degenerative Lamellar Macular Hole; Lamellar Macular Hole; Premacular membrane; macular pucker; epiretinal proliferation; epiretinal membrane; pars plana vitrectomy.

Summary Statement:

Pars plana vitrectomy with membrane peeling in the treatment of tractional lamellar macular holes/macular pseudoholes (LMH/MPH) and degenerative LMH has greater functional improvement in the tractional LMH/MPH subgroup. Complete postoperative anatomical restoration occurred in the majority of tractional LMH/MPH lesions, but not in degenerative LMH.

Abstract

Purpose: Functional and anatomic outcomes of vitrectomy with membrane peeling were compared in tractional lamellar macular holes (LMH)/Macular pseudoholes (MPH) versus degenerative LMH.

Methods: This multicenter retrospective study enrolled patients with a minimum follow-up of 6 months. The association of spectral-domain optical coherence tomography (SD-OCT) parameters with pre- and postoperative best-corrected visual acuity (BCVA) was analyzed.

Results: Seventy-seven (74.8%) tractional LMH/MPH, and 26 (25.2%) degenerative LMH were included. Preoperative BCVA was better in tractional LMH/MPH (0.39±0.2 logMAR, 20/50 Snellen Equivalent) than degenerative LMH (0.56±0.2 logMAR, 20/66 Snellen Equivalent; p<0.001). Premacular membranes (PMM) were found in all tractional LMH/MPH, while LMH associated epiretinal proliferation (LHEP) was present in all degenerative LMH. Primary anatomic success was achieved in 97/103 eyes (94.2%), with foveal restoration occurring earlier in degenerative LMH (1.6±2.3 VS 3.3±3.6 months; p=0.025). BCVA improved in both tractional LMH/MPH and degenerative LMH (p<0.001 and p=0.012, respectively), but was better in tractional LMH/MPH (p=0.001).

Conclusions: The presence of PMM and absence of LHEP in all tractional LMH/MPH further distinguishes this from degenerative LMH. BCVA improved in both subgroups, but more so in tractional LMH/MPH. Complete anatomic restoration of foveal microanatomy was rare in degenerative LMH, reflecting significant morphological and pathophysiological differences between the two lesions.

INTRODUCTION

The diagnosis “lamellar macular hole” (LMH) currently includes a heterogeneous group of macular lesions which share common morphologic features such as partial thickness defects in the fovea, irregular foveal contour, and characteristic autofluorescence patterns.[1,2]

Since the original description of LMH by Gass in 1976, major advances in fundus imaging have led to transformational changes in our understanding of this pathology.[3] Specifically, the introduction of high-definition spectral-domain optical coherence tomography (SD-OCT) technology allowed clinicians to study LMH *in vivo* with an unprecedented level of detail.[1] However, with SD-OCT the distinction between LMH and other macular conditions such as macular schisis or pseudohole became controversial.[4] Consequently, the definition itself of LMH is not uniform in the literature, and it has further changed with improvements in SD-OCT imaging.[5]

Recently, Govetto et. al proposed the distinction between two subtypes of LMH, tractional and degenerative, arguing that they may represent different pathologic conditions with similarly different clinical implications.[5] The degenerative LMH has a “top hat” morphology on SD-OCT and it is characterized by the frequent presence of a “thick” or “dense” premacular membrane (PMM), recently renamed lamellar macular hole associated epiretinal proliferation (LHEP) by Pang et al.[6] This subtype of LMH is also characterized by intra-retinal cavitation potentially involving all retinal layers, especially compromise of the foveal photoreceptors (figure 1, A). Tractional LMH is characterized by a “moustache” appearance on SD-OCT. This subtype of LMH is defined by a sharp split at the level of the Henle fiber layer and by the presence of a PMM with little cellularity, while foveal photoreceptors are often spared (figure 1, B).

However, some authors do not consider tractional LMH to be a “true” LMH but rather a macular pseudohole (MPH) with lamellar cleavage, due to the apparent lack of tissue loss.[4] Thus, in view of the absence of universal consensus and ongoing controversy on LMH definition and classification, the authors chose to adopt more inclusive terminology: in this work, the terms “tractional” LMH and “macular pseudohole” (MPH) were both used to refer to those lesions with PMM, foveal traction and macular schisis, while the term “degenerative LMH” was employed for those lesions with LHEP.

To date, there is no consensus regarding the treatment of tractional LMH/MPH and degenerative LMH, as published data does not provide any clear recommendations.[5] In fact, some contend that observation is preferable to surgery, as these lesions have been shown to be relatively stable over time.[5,7] Yet, surgical intervention with pars plana vitrectomy (PPV) and peeling of PMM or LHEP may be considered in clinically significant cases with visual acuity deterioration or anatomic progression.[7] However, few studies have investigated surgical outcomes in eyes with degenerative LMH versus tractional LMH/MPH, and the published results are somewhat controversial, particularly in those lesions with LHEP.[8-10] Indeed, while dell’Omo et al. and Lai et al. reported that the presence of LHEP does not seem to influence the natural course of LMH and the response to surgery,[8,9] their conclusions were not confirmed in a subsequent study by Ko et al.[10]

Therefore, this study performed in-depth analyses of functional and anatomic surgical results after PPV with peeling of the PMM or LHEP in patients diagnosed with degenerative LMH as compared to tractional LMH/MPH.

MATERIAL AND METHODS

This retrospective observational study was approved by the Institutional Review Boards of the Ramon y Cajal University Hospital (Spain), the Sunderland Eye infirmary (UK), the University of California Los Angeles (USA). This research project adhered to the tenets of the Declaration of Helsinki and was designed in compliance with the Health Insurance Portability and Accountability Act regulations.

The clinical records and SD-OCT images of patients diagnosed with either tractional LMH/MPH or degenerative LMH between January 1, 2010 and January 1, 2017 were evaluated by four retina specialists (M.S.F., D.S., J.S. and J.P.H.) at the the Ramon y Cajal University Hospital, the Sunderland Eye infirmary, the Stein Eye Institute and the VMR Institute for Vitreous Macula Retina. In two participating centers, cases were identified by a medical billing record search, using the International Statistical Classification of Diseases and Related Health Problems, Ninth Revision (ICD-9) diagnosis codes 362.56 for macular pucker and 362.54 for macular cysts, holes, and pseudoholes. At the Ramon y Cajal University Hospital (Spain) and at the Sunderland Eye Infirmary (UK) the search was carried out manually using proprietary medical database.

Inclusion criteria were the presence of tractional LMH/MPH and degenerative LMH treated with PPV and peeling of PMM or LHEP, with a minimum follow-up of 6 months and preoperative as well as postoperative SD-OCT imaging. Exclusion criteria were history of advanced age-related macular degeneration, advanced glaucoma, diabetic retinopathy and other vascular retinal diseases, myopic choroidal neovascularization, macular telangiectasis, retinal dystrophies, uveitis and intraocular infections, trauma, and any previous intraocular surgery apart from uncomplicated cataract surgery.

Comprehensive ophthalmologic exams included best-corrected visual acuity (BCVA) assessment, measurement of intraocular pressure, slit-lamp biomicroscopy, and fundus examination. BCVA was recorded at each visit, reported in Snellen fraction and then converted into logarithm of the minimal angle of resolution (logMAR) values for statistical analysis.

SD-OCT images were obtained with either the Spectralis OCT with eye-tracking dual-beam technology (Heidelberg Engineering GmbH, Heidelberg, Germany) or with the Cirrus HD-OCT 5000 (Carl Zeiss Meditec AG, Oberkochen, Germany) or the Optos SD-OCT/SLO (Optos, Marlborough, Mass, USA). Spectralis OCT scans were analyzed with the Heidelberg Eye Explorer (version 1.8.6.0) using the HRA/Spectralis Viewing Module (version 5.8.3.0), while Cirrus OCT scans were analyzed with the Cirrus review software Version 8.0.

With Spectralis OCT, at each visit all eyes were imaged with at least 2 type of SD-OCT scan patterns: 19 B-scans administered over an area of 20 X 15 degrees with each B-scan spaced 242 µm apart and a single high-definition horizontal B-scan at 30 degrees. In addition, some of the included eyes underwent high-density scanning over a macular area of either 15 X 10 degrees with 97 B-scan each spaced 31 µm apart, or 15 X 5 degrees with 131 B-Scan spaced 11 µm apart. With Cirrus OCT, each eye was imaged with the Macular cube 518 x 128 scans and with the HD 5-line raster. Mean central foveal thickness (CFT) values were obtained automatically by the Heidelberg, Zeiss, and Optos proprietary software. Tractional LMH/MPH and degenerative LMH were identified with SD-OCT, defined according to Govetto et al. as illustrated in figure 1.[5] A PMM was defined as a single, irregular, and hyper-reflective line above the inner limiting membrane (ILM), often associated with signs of tangential traction (retinal wrinkling) and with the occasional presence of hyporeflective spaces between the PMM and ILM (figure 2, A). LHEP was defined as thick and uniform iso-reflective material located above the ILM, covered by a thin hyperreflective line without signs of wrinkling in the underlying retina and without the presence of hypo-reflective spaces between LHEP and the ILM (figure 2, B).

Intraretinal cavitation was defined with SD-OCT as the presence of confluent and round hyporeflective intraretinal spaces potentially involving all retinal layers, with the occasional presence of septae of residual retinal tissue. Intraretinal schisis was defined with SD-OCT as a sharp separation between inner and outer retinal layers with a split located between the outer nuclear layer (ONL) and outer plexiform layer (OPL), at the level of the Henle fiber layer. Intraretinal schisis was also characterized by the presence of multiple hypo-reflective intraretinal spaces, separated by hyper or iso-reflective bridges of retinal tissue.

The presence of a discontinuous ellipsoid or external limiting membrane (ELM) band in the foveal region was considered a sign of photoreceptor compromise and outer retinal disruption.

All patients underwent a standard, three ports 23 or 25-Gauge PPV with PMM or LEHP peel performed by four vitreo-retinal surgeons (M.S.F., D.S., J.S., J.P.H.) with the Constellation vision system (Alcon, Fort wort, TX, USA). ILM removal and combined phacoemulsification cataract surgery were performed at the discretion of the surgeon. Core vitrectomy was performed in all cases. After the creation of posterior vitreous detachment, ILM forceps were used to peel the PMM or LHEP and, in some cases, the ILM up to the vascular arcades. Based on the surgeon’s discretion, the use of either intraocular Kenalog (Bristol-Myers Squibb, Irvine, CA, USA), Brilliant blue G (DORC, Zuidland, The Netherlands) or indocyanine green (ICG) was applied over the retinal surface to enhance visualization during ILM peeling. At the end of surgery, the eyes were filled with balanced saline solution (BSS), air, octafluoropropane (C3F8), or sulfur-hexafluoride (SF6).

All patients were evaluated at least at 1 and 6 months after surgery, and potential post-operative complications were recorded at any time point during the follow up period. Primary anatomic success was defined as the absence of breaks in the inner fovea and the disappearance of either intraretinal cavitation or macular schisis (i.e. absence of any intraretinal hyporeflective spaces as seen with SD-OCT) after a single surgical procedure.

Two courses of post-operative healing were observed: delayed and immediate. Delayed healing was defined as persistence of intraretinal hyporeflective spaces in the foveal region beyond the first month following surgery, with their progressive disappearance during the follow-up period (figure 3). Immediate healing was defined as the complete disappearance of all intraretinal hyporeflective spaces in the foveal region at one month following surgery (figure 4).

Mean and standard deviations were calculated for continuous variables, while frequency and percentages were calculated for categorical variables. Student's t-test was used to compare the statistically significant difference in continuous measurements among all subgroups, Chi-square test was used to compare proportions among the study groups. The association of SD-OCT parameters with BCVA was assessed by means of univariate and multivariate linear or logistic regression, as appropriate. Log-range test was used to compare the survival functions of the two subgroups of LMH (i.e. anatomical restoration) in Kaplan-Meier survival curves. All analyses were conducted using Stata 15.1 software (StataCorp, College Station, TX, USA).

RESULTS

Preoperative findings:

After the review process, this study enrolled 103 eyes of 103 patients, of whom 38 were males (37%) and 65 were females (63%) with a mean age at surgery of 67 ± 8.9 years (range 31-89) and a mean follow-up of 30.8 ± 28.8 months (range 6-96 months). At presentation, 52 out of 103 eyes (50.5%) were phakic, while the remaining 51 (49.5%) were pseudophakic.

Tractional LMH/MPH was diagnosed in 77 out of 103 eyes (74.8%), while degenerative LMH was diagnosed in 26 out of 103 eyes (25.2%) without significant differences in gender and age between the two LMH subgroups.

Preoperative mean BCVA in the tractional LMH/MPH subgroup was 0.39 ± 0.2 LogMAR (20/50 Snellen equivalent), while the degenerative subgroup BCVA was 0.56 ± 0.2 LogMAR (20/72 Snellen equivalent), $p<0.001$. A PMM was present in all tractional LMH/MPH (77 out of 77 eyes, 100%), while LHEP was found in all degenerative LMH (26 out of 26, 100%). Only 1 out of 77 eyes with tractional LMH/MPH had both PMM and LHEP. No PMM was diagnosed in degenerative LMH eyes.

Preoperatively, 13 out of 26 eyes (50%) diagnosed with degenerative LMH had outer retinal disruption, which was present in only 11 out of 77 eyes (14.3%) diagnosed with tractional LMH/MPH; $p<0.001$. In the tractional LMH/MPH subgroup the mean CFT was 24.6% thicker ($p=0.016$) than the degenerative LMH subtype (279.1 ± 108 µm, range 254-303 µm; versus 224 ± 66 µm, range 197-250 µm).

Surgical intervention:

Twenty-three-gauge PPV was preferred in most of the cases (85 out of 103 eyes, 82.5%), while in the remaining 18 eyes (17.5%) 25-gauge PPV was performed. Combined phacoemulsification with intraocular lens implantation was performed in 13 out of 103 eyes (12.6%).

Double peeling of PMM or LHEP and ILM was performed in the vast majority of eyes (99 out of 103 eyes, 96.1%), while in the remaining 4 cases (3.9%) just the PMM was removed. The ILM was stained with Brilliant Blue G in 66 out of 99 cases (66.6%), and with ICG in 16 out of 99 eyes (16.2%), while in the remaining 15 eyes (15.2%) chromodissection was not performed.

Fifteen out of 103 eyes (14.6%) were filled with BSS at the end of the surgery. Gas tamponade with C_3F_8 was performed in 32 out of 103 eyes (31.1%), while in 31 out of 103 eyes (30.1%) SF_6 tamponade was preferred. The remaining 25 eyes (24.2%) were partially filled with air.

Intraoperative complications (i.e. iatrogenic retinal break during ILM peel and a choroidal detachment) were encountered in 2 out of 103 eyes (1.9%).

Postoperative anatomic outcomes:

Primary anatomic success was achieved in 97 out of 103 eyes (94.2%), in which either intraretinal cavitation or macular schisis disappeared post-operatively. Surgical intervention was not able to achieve foveal anatomy restoration in 5 tractional LMH/MPH and in 1 degenerative LMH (5.8%), in which there was persistent intraretinal cavitation/macular schisis until the end of the follow-up period. The Kaplan-Meier estimate of the probability to miss primary anatomic success was 36% (95%CI:

27-45%) at 1 month, 17% (95%CI: 10-24%) at 6 months and 3% (95%CI: 0-8%) for those LMH with 12 months follow-up.

Postoperative healing times differed significantly between the two LMH subtypes ($p<0.001$): delayed healing was more frequent in tractional LMH/MPH (37 out of 72 eyes, 51.4%) while immediate healing was prevalent in the degenerative subtype (22 out of 25 eyes, 88%), as illustrated in figure 3 and 4. Kaplan-Meier survival analysis confirmed significant differences between tractional LMH/MPH and degenerative LMH ($p=0.025$) as illustrated in figure 5, A: the tractional LMH/MPH subtype appeared to heal more slowly after surgery (mean time to primary anatomic success 3.3 ± 3.6 months, range 1-14 months) as compared to the degenerative group (mean time to primary anatomic success 1.6 ± 2.3 months, range 1-12 months).

Outer retinal disruption resolved postoperatively in 7 out of 24 eyes (5 tractional LMH/MPH and 2 degenerative LMH, 29.2%), while in the remaining 17 eyes (6 tractional LMH/MPH and 11 degenerative LMH, 70.8%) ellipsoid and/or ELM alterations persisted up to the end of the follow-up period.

The type of tamponade did not significantly change postoperative anatomic success rates and LMH healing time ($p=0.064$); see Kaplan-Meier survival analysis in figure 5, B.

The rate of postoperative complications was low, as they were encountered in only 5 out of 103 eyes only (4.8%): 3 cases (two degenerative LMH and one tractional LMH/MPH) developed full thickness macular holes after a mean follow-up of 8 ± 1.7 months. In the remaining 2 eyes, both degenerative LMH, a rhegmatogenous retinal detachment developed 6 months after surgery. In both cases retinal breaks were located in the periphery, without macular involvement in the retinal detachment.

At the end of the follow up-period most eyes were pseudophakic, with no significant differences among the tractional LMH/MPH (22 out of 26 eyes, 84.6%) and the degenerative LMH (64 out of 77 yes, 83.1%) subgroups, with a p-value = 0.859.

Postoperative functional outcome and correlations with SD-OCT parameters

As illustrated in figure 6, BCVA improved in both degenerative LMH and tractional LMH/MPH ($p<0.001$ and $p=0.012$, respectively). At the end of the follow-up period of 30.8 ± 28.8 months, BCVA differences between the two groups remained significant ($p<0.001$). After adjusting for preoperative BCVA, there was still more postoperative visual acuity improvement in tractional LMH/MPH as compared to degenerative LMH ($p=0.006$). Changes in BCVA over the follow-up period are summarized in table 1. Having delayed, rather than immediate healing was not associated with significant differences in postoperative visual recovery, even adjusting for baseline BCVA ($p=0.118$). In eyes with delayed healing, BCVA improved significantly with the disappearance of the break in the inner fovea ($p=0.002$) and continued to increase with the disappearance of the intraretinal schisis/cavitation up to the end of the follow up period ($p=0.001$). In both univariate and multivariate logistic regression models, worse preoperative BCVA and preoperative outer retinal disruption were significantly associated with lower postoperative visual recovery ($p<0.010$ for all coefficients).

DISCUSSION

The optimal management of patients diagnosed with LMH is controversial, and observation is often preferred to surgery due to the relative anatomic and functional stability of these lesions.[2,5] However, a more interventional attitude may be necessary in cases with signs of anatomic and/or functional deterioration, or if preoperative vision is causing significant disability.[2,8-10]

This study analyzed the postoperative functional and anatomic outcomes of vitrectomy with membrane peeling in a large series of patients diagnosed with tractional LMH/MPH and degenerative LMH, and found high rates of anatomic restoration and significant improvement in visual acuity of both subtypes. However, improvements were significantly greater in tractional LMH/MPH, as compared to degenerative LMH. This fact is not surprising given that degenerative LMH cases were characterized by worse preoperative BCVA and higher rates of preoperative ellipsoid/ELM disruption, consistent with previous reports.[2,5,8-13] Indeed, such preoperative features are robust indicators of worse postoperative functional improvement in all vitreo-macular surgery.[14]

In the published literature, postoperative findings in LMH are heterogeneous: dell'Omo and associates and Lai et al. reported that the presence of LHEP does not seem to influence the natural course of the disease or the response to surgery, as compared to eyes without LHEP.[8,9] Contrastingly, Ko et al. found that BCVA significantly improved after surgery in eyes without LHEP, but showed no change in eyes with LHEP.[10] The variability of such results may be due to the absence of consensus on the definition and classification of LMH, which complicates inter-study comparisons.[5]

The differing postoperative healing rates (delayed versus immediate) seen in tractional LMH/MPH and degenerative LMH might be explained by the morphological and pathophysiological differences between these lesions. In degenerative LMH, there is no mechanical separation between inner and outer retina, but rather loss of retinal tissue due to presently unknown pathophysiological mechanisms, with the subsequent accumulation of LHEP in the foveal region.[5] With the removal of the ILM and the LHEP, the residual inner retinal tissue might be free to settle over the foveal floor, with the disappearance of cavitations (immediate healing illustrated in figure 3). In tractional LMH/MPH, mechanical forces exerted by the PMM onto the inner retinal surface cause the elongation and verticalization of the axons of the Müller cells in the Henle fiber layer, resulting in a schisis morphology.[5] With PPV, PMM and ILM peeling such traction is relieved, and the axons of the Müller cells can return to their original morphology, with the restoration of macular anatomy and the disappearance of the macular schisis (delayed healing, illustrated in figure 4).

In the present study, qualitative analysis of the postoperative foveal microstructure also showed significant differences between the two subtypes of LMH. After surgery the majority of tractional LMH/MPH, recovered foveal microstructure almost completely, without evidence of disruption in retinal layers and/or apparent tissue loss (figure 4). This confirms the hypothesis that tractional LMH/MPH is characterized by displacement rather than loss of retinal tissue.[4,5] Contrastingly, postoperative foveal microstructure in degenerative LMH was disrupted in the majority of cases, further distinguishing these two lesions (figure 3). In degenerative LMH cavitation loss was replaced by mid-reflective material on OCT, similar to LHEP.

Limitations of this study include its retrospective nature, which may have caused some bias. Moreover, this was not a single-surgeon series, a fact which could have caused data heterogeneity. Also, no imaging of the vitreo-papillary interface was undertaken, although previous studies identified a higher prevalence of vitreo-papillary adhesion (VPA) in LMH than macular pucker, but lower than full-thickness macular holes.[15,16] Future studies should explore the relative prevalence of VPA in tractional LMH/MPH vs. degenerative LMH and integrate this information into our fund of knowledge about these two LMH subtypes. Strengths of this study include the adequate size of the study population, which increased the power of statistical analyses, and the long duration of follow up.

To conclude, this study analyzed the anatomic and functional results of PPV with PMM or LHEP peeling in a large series of tractional LMH/MPH and degenerative LMH. BCVA improved significantly in both lesions, although functional improvements were greater in the tractional LMH/MPH. Rates of healing differed with delayed healing common in tractional LMH/MPH, and immediate healing in degenerative LMH. Complete anatomic restoration of foveal microanatomy was observed in the majority of the tractional LMH/MPH but not in the degenerative subtype, probably reflecting significant morphological and pathophysiological differences between the two LMH subtypes. Thus, the results presented herein support current thinking which considers tractional LMH/MPH and degenerative LMH as two distinct clinical entities.[4,5] However, the authors stress the compelling need for uniform terminology and definitions of LMH, MPH and similar macular lesions, which would simplify the design of future research and communication among clinicians.

Future larger and prospective investigations employing uniform and universally accepted disease classifications and terminology are needed to reduce bias and to better understand the effectiveness of surgical treatment with and PMM or LHEP peeling for both tractional LMH/MPH and degenerative LMH.

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FIGURE CAPTIONS:

Figure 1: Degenerative and tractional lamellar macular holes / macular pseudoholes. A: Degenerative lamellar macular hole. This subtype of lamellar macular hole has a "top hat" morphology and it is associated with the presence of lamellar macular hole associated preretinal proliferation. These lesions present with intraretinal cavitation, potentially affecting all retinal layers. A foveal "bump" of spared retinal tissue is frequently present, as well as outer retinal disruption. **B. Tractional lamellar macular hole/macular pseudohole.** This subgroup of lamellar macular hole has a "moustache" morphology, and it is associated with the presence of premacular membranes. These lesions present with a "schitic" morphology, with a sharp split located in the Henle fiber layer, which separates inner and outer retina. Foveal photoreceptors are frequently spared.

Figure 2: Differences between lamellar macular hole associated epiretinal proliferation (LHEP) and premacular membrane (PMM) without proliferation. A. LHEP. LHEP (black arrows) appears on SD-OCT as a thick isoreflective preretinal formation, covered by a thin hyperreflective line. The LHEP is always in direct contact with the inner limiting membrane, and no signs of retinal wrinkling are present. **B. PMM.** Premacular membrane (white arrows) is visible with SD-OCT as a sharp hyperreflective line, frequently associated with multiple hyporeflective empty spaces between the membrane and the inner limiting membrane (white star). Wrinkling of the underlying retina is evident.

Figure 3: Immediate healing. A. Preoperative appearance. A degenerative lamellar macular hole is diagnosed with spectral-domain optical coherence tomography. **B.**

Postoperative appearance at 1 month. Intraretinal cavitation disappeared, but the foveal microstructure appears disrupted.

Figure 4: Delayed healing. A. Preoperative appearance. A tractional lamellar macular hole/macular pseudohole is diagnosed with spectral domain optical coherence tomography (SD-OCT). **B. Postoperative appearance at 1 month.** The foveal break is closed, but intraretinal hyporeflective spaces are still visible with SD-OCT. **C. Postoperative appearance at 2 months.** Foveal thickness decreased, intraretinal hyporeflective spaces reduced, but are still visible with SD-OCT. **D. Postoperative appearance at 3 months.** At three months, intraretinal hyporeflective spaces disappeared, and the foveal microanatomy is restored.

Figure 5. Kaplan-Meier Analyses of Healing Rates. A. Tractional lamellar macular hole/macular pseudohole versus degenerative lamellar macular hole. Delayed healing is common in the tractional lamellar macular hole (LMH)/macular pseudhohole (MPH) subtype, as compared to the degenerative LMH. Therefore, the tractional LMH/MPH subtype appeared to heal significantly more slowly after surgery. **B. Healing rates accorwith different intraocular tamponade.** There are no significant differences in healing rates among different endotamponade agents.

Figure 6. Preoperative and Postoperative best corrected visual acuity in tractional lamellar macular holes/macular pseudoholes and degenerative lamellar macular holes. In both tractional lamellar macular holes/macular pseudoholes and degenerative lamellar macular holes, best-corrected visual acuity significantly improved after surgery.

Figure 1

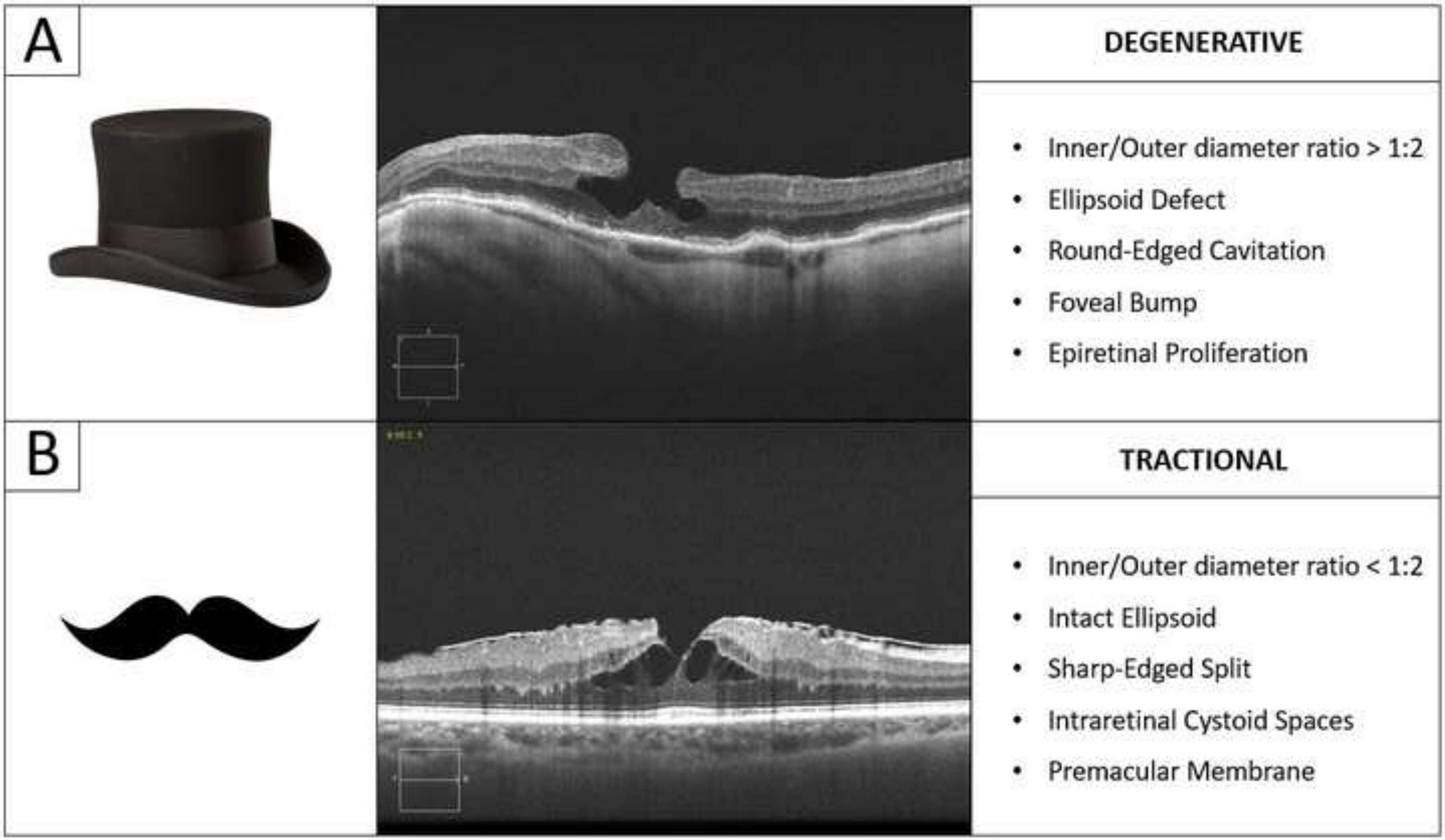
A
DEGENERATIVE
• Inner/Outer diameter ratio > 1:2
• Ellipsoid Defect
• Round-Edged Cavitation
• Foveal Bump
• Epiretinal Proliferation
B
TRACTIONAL
• Inner/Outer diameter ratio < 1:2
• Intact Ellipsoid
• Sharp-Edged Split
• Intraretinal Cystoid Spaces
• Premacular Membrane

Figure 2

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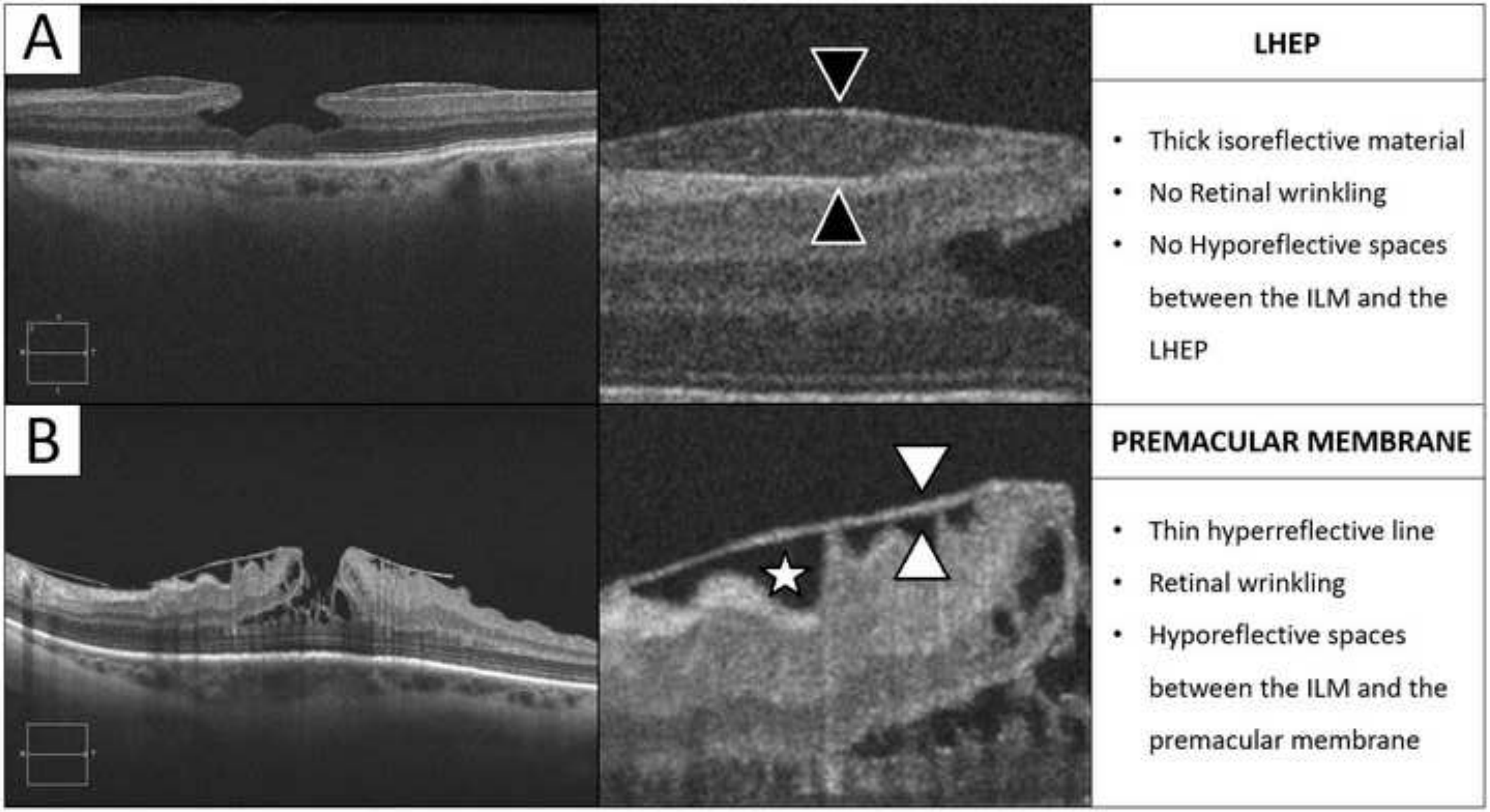

Figure 3

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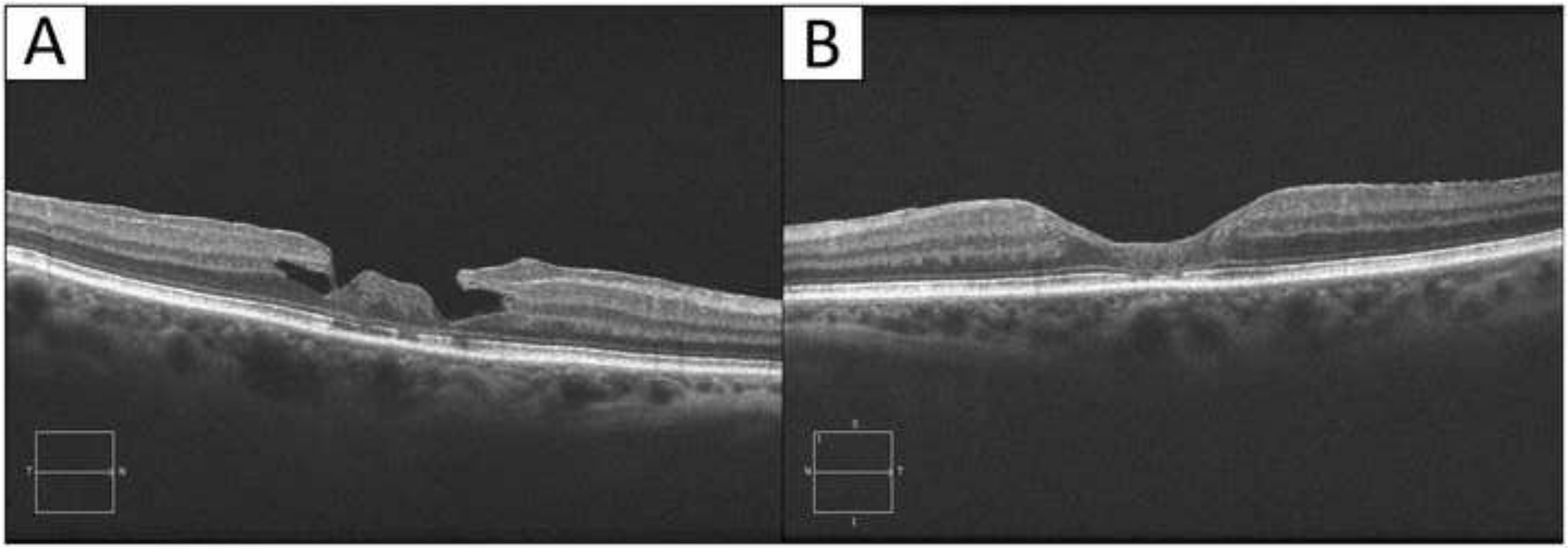

Figure 4

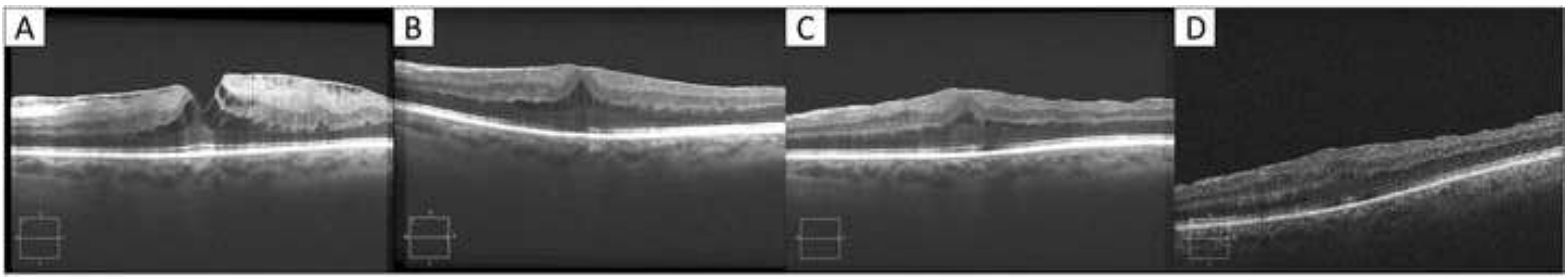

Figure 5

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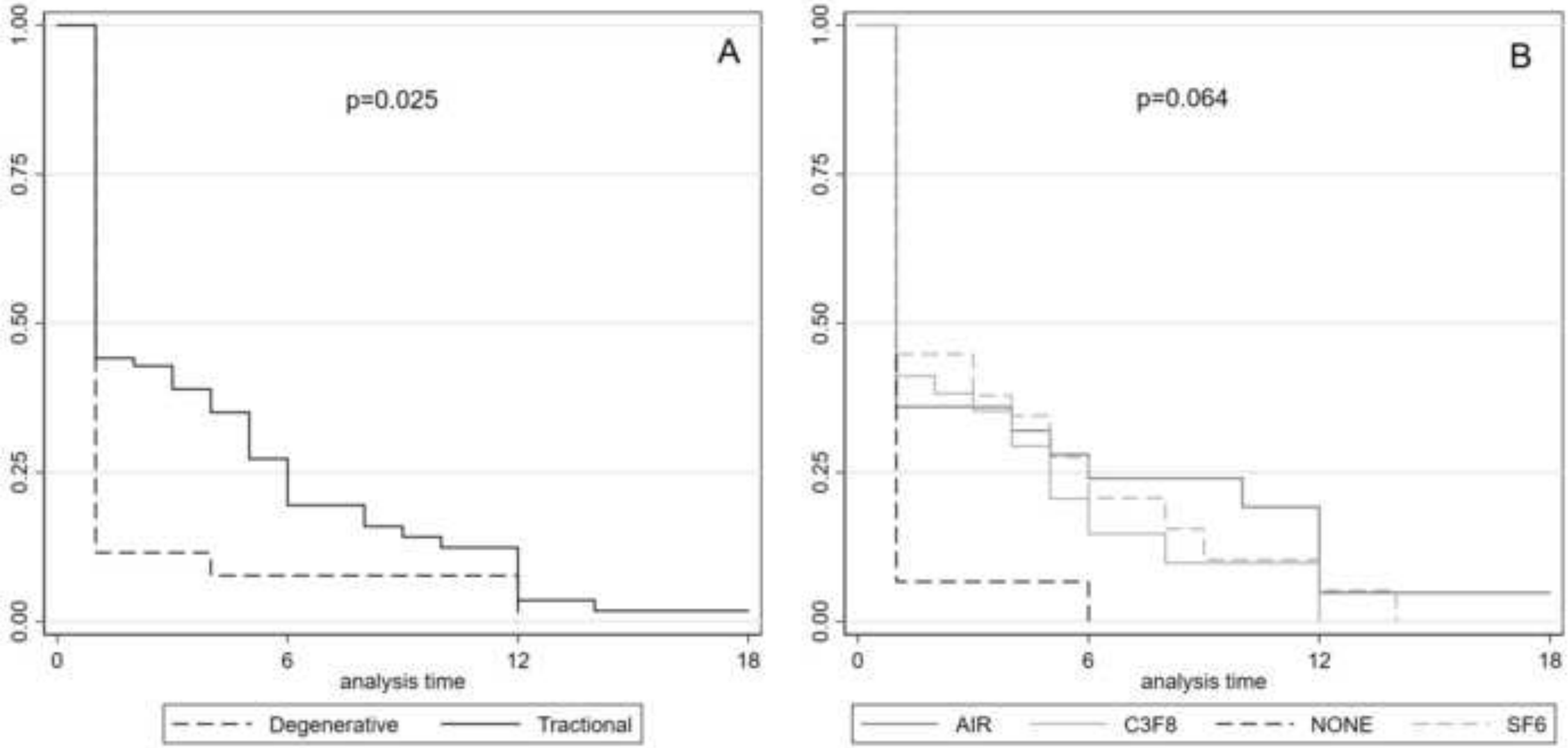

Figure 6

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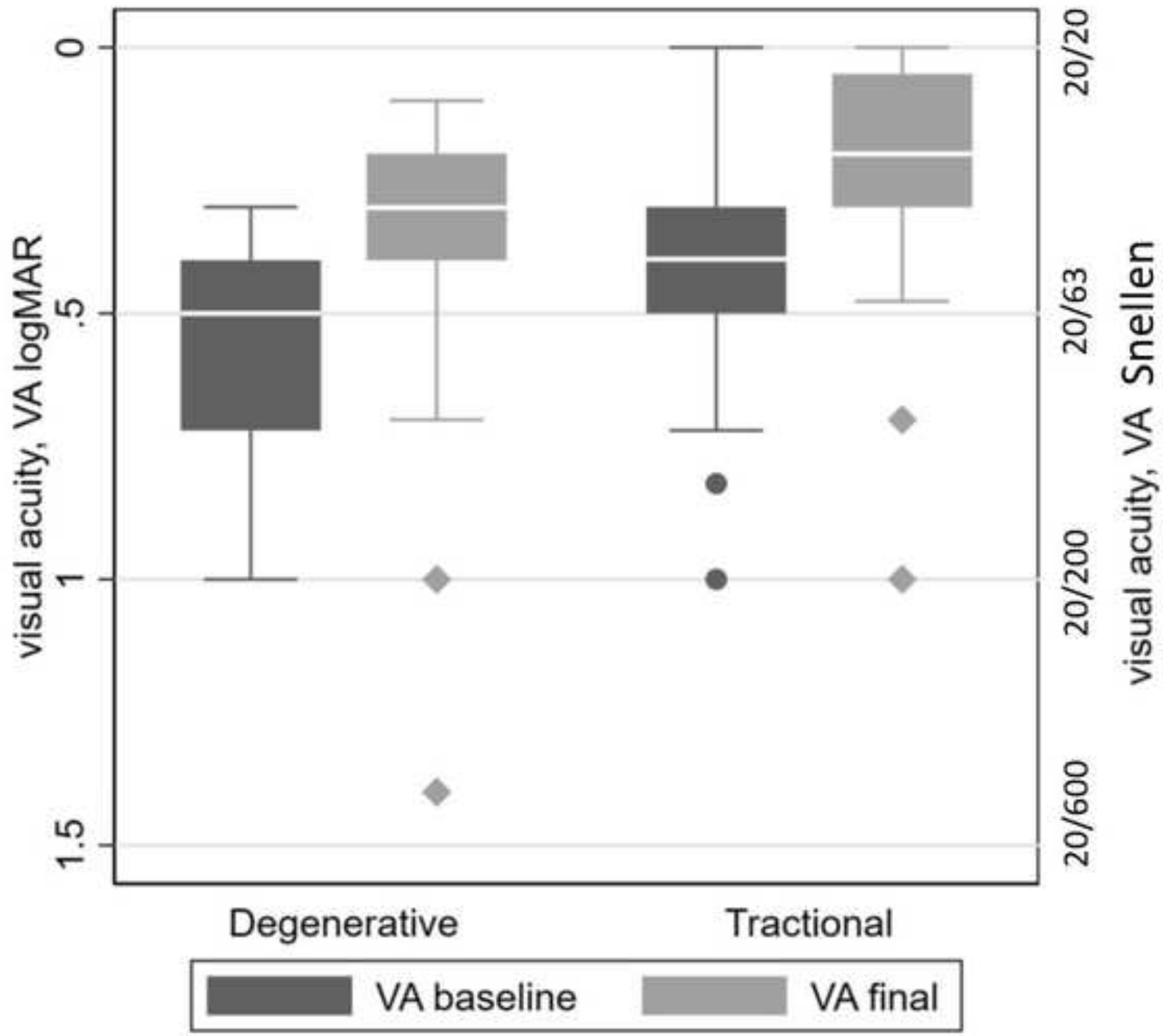

Table 1: Preoperative and postoperative best corrected visual acuity

	Preoperative BCVA	Postoperative BCVA	p-value
Tractional LMH/MPH	0.38 ± 0.19 LogMar (20/48 Snellen Equivalent)	0.18 ± 0.17 LogMar (20/30 Snellen Equivalent)	0.012
Degenerative LMH	0.56 ± 0.19 LogMar (20/72 Snellen Equivalent)	0.39 ± 0.28 LogMar (20/50 Snellen Equivalent)	<0.001
p-value	<0.001	<0.001	

BCVA: Best corrected visual acuity; PMM: Premacular membrane; LMH: lamellar macular hole; MPH: Macular pseudohole.